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10/758,562	01/16/2004	Akira Saito	Q79447	5978

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EXAMINER

JOYCE, CATHERINE

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/758,562

Applicant(s)

SAITO ET AL.

Examiner

Catherine M. Joyce

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 June 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5, 7 and 9-21 is/are pending in the application.
- 4a) Of the above claim(s) 3, 4, 11-14, and 19-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 8/24/05

- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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1. Claims 1-5, 7, and 9-21 are pending, and claims 3, 4, 11-14, and 19-21 are withdrawn from consideration as being drawn to a non-elected invention
2. Claims 1, 2, 5, 7, 9-10, and 15-18 are under examination.
3. Applicant's election of the invention Group I, and the species 1 (SEQ ID NO:8 and SEQ ID NO:9, corresponding to claim 18), in the reply filed on June 8, 2006 is acknowledged. Because Applicant did not point out any errors in the restriction requirement, the election is treated as an election without traverse.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to

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make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to the following:

a process for producing a recombinant polypeptide or its salts comprising the amino acid sequence of SEQ ID NO:1 comprising the steps of:

transforming a host cell with a recombinant vector comprising a polynucleotide encoding the polypeptide represented by SEQ ID NO:1, thereby creating a transformed cell;

culturing the transformed cell whereby the transformed cell produces said polypeptide; and

collecting said recombinant polypeptide from the culture (claim 9);

a process for producing a recombinant oncogenic protein comprising an amino acid sequence of SEQ ID NO:1 comprising the steps of:

transforming a host cell with a recombinant vector comprising a polynucleotide encoding an oncogenic protein with the amino acid sequence of SEQ ID NO:1, thereby creating a transformed cell;

culturing the transformed cell whereby the transformed cell produces said recombinant oncogenic protein; and

collecting said recombinant polypeptide from the culture (claim 10);

The specification teaches the cloning and sequencing of a human cDNA encoding a hWAPL protein using a human testicular cDNA kit (Example 1). The

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specification also teaches that among carcinoma cells examined of cervical cancer, corpus uteri cancer, ovarian cancer, gastric cancer, renal cancer, pulmonary cancer, colorectal cancer, and breast cancer, about 40% of carcinoma cell samples of cervical cancer demonstrated significant hWAPL gene expression and that some gastric cancers also demonstrated high expression of the hWAPL gene (Example 2). The specification also teaches that transfection of a human epidermal cell line (HDK1) to express the HPV E6 gene product resulted in cleavage of the p53 tumor suppressor protein and expression of the hWAPL gene (Example 3). The specification also teaches that when cell lines CaSki, SiHa and C33A were transfected with MSCV-puro BPV1E2, CaSki and SiHa cell lines producing E6 and E7 from HPV16 demonstrated increase of the remained p53 tumor suppressor protein as a result of inhibiting transcription of E6 and E7 genes by the E2 from HPV, with concomitant inhibition of expression of the hWAPL, whereas in the C33A cell line, in which cancerization is induced by mechanisms other than by HPV infection, remain levels of the p53 protein or expression levels of hWAPL protein were unaffected (Example 3). The specification also teaches that transforming a HeLa cells with a p53 expression vector reduced that amount of luciferase reporter protein that was producing using a hWAPL promoter attached to the luciferase gene (Example 4). The specification also teaches the construction of an expression vector for producing hWAPL fused to a green fluorescent protein and the transfection of a host mammalian cell with the vector with concomitant selection, wherein a transformed host cell line carrying the desired expression vector for expressing the hWAPL protein was obtained (Example 5). The specification also teaches that a HeLa cell infected with the an expression vector for the hWAPL-green fluorescent protein fusion is selected to select cells positive and negative for hWAPL protein expression, wherein cells that a negative of hWAPL protein expression show a chromosome gene content similar to that of the host HeLa cells whereas cells that are positive for hWAPL protein expression show an increase in the amount of polyploidy chromosomes and the induction of multi-nucleation (Example 7). The specification also teaches that NIH 3T3 cells that were transfected with an expression vector for hWAPL, with western blot confirmation of protein expression, form a focus structure in cell

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culture whereas control cells form a single-cell confluent layer, and that the transfected cells that were injected into mice were oncogenic (Example 8). The specification also teaches that a small inhibitory RNA that was targeted to the hWAPL gene inhibited cell growth of SiHa cervical cancer cell line, that the SiHa cell lines formed tumors in mice, and that injection of the tumors with a siRNA resulted in a reduction in tumor size (Example 9).

The teaching of the specification cannot be reasonably extrapolated to enable the claims because the teaching in the specification (i) that the RNA encoding the hWAPL protein is expressed in human cancers and (ii) that transfection of a cell line with the hWAPL gene is not sufficient to establish that the hWAPL protein is oncogenic or is involved in cancer in humans, and thus one of skill in the art would not know how to use the protein produced by the claimed method.

In the first aspect, one of skill in the art cannot extrapolate the teaching of the specification to the enablement of the claims because the specification does not teach that the hWAPL polypeptide is expressed in any cancer cells. The prior art is replete with examples in which expression levels of mRNA are not correlated with expression levels of the encoded protein. For example, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Brennan et al (Journal of Autoimmunity, 1989, vol. 2 suppl., pp. 177-186) teaches that high levels of the mRNA for TNF-alpha were produced in synovial cells, but that levels of the TNF alpha protein were undetectable, and Zimmer (Cell Motility and the Cytoskeleton, 1991, vol. 20, pp. 325-337) teaches that there is no correlation between the mRNA level of calcium-modulated protein S100 alpha and levels of S100 alpha protein. Eriksson et al. (Diabetologia, 1992, vol. 35, pp. 143-147) teaches that no correlation is observed between levels of mRNA transcripts encoding the insulin-responsive glucose transporter and expression levels of the protein. Thus, observation of expression of mRNA does

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not appear to be predictive of concomitant expression of protein. Thus, given the state of the art as reviewed above, data on the expression of mRNA encoding the hWAPL polypeptide in cancer cells does not allow one of skill in the art to predict that the hWAPL polypeptide is expressed in tumor cells or is involved in oncogenesis *in vivo*.

In the second aspect, one of skill in the art cannot extrapolate the teaching of the specification to enable the claim because the teaching in the specification that expression of the hWAPL protein in a cell line results in oncogenesis is not sufficient to establish that the hWAPL protein is associated with oncogenesis *in vivo*. In particular, Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teaches that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Further, Dermer (Bio/Technology, 1994, 12:320) teaches that, a petri dish cancer is a poor representation of malignancy, with characteristics profoundly different from the human disease. Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary -type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not, yet normal or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions. Thus, given the state of the art as

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reviewed above, data on the oncogenesis inducing potential of the expression of an hWAPL polypeptide in a cell line does not allow one of skill in the art to predict that the hWAPL polypeptide is expressed in tumor cells or is involved in oncogenesis.

It is clear that based on the state of the art, in the absence of experimental evidence, one skilled in the art would accept the assertion that the hWAPL protein is expressed in cancer cells or is involved in oncogenesis in vivo. The specification provides insufficient guidance with regard to this issue and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the hWAPL protein is expressed in cancer cells or is involved in oncogenesis in vivo. Thus, one of skill in the art would not know how to use the invention and practice of the invention would require undue experimentation.

6. Claims 1, 5, and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:2, does not reasonably provide enablement for an isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO:1.

The claims are drawn to the following:

an isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide represented by SEQ ID NO:1 (claim 1);

a recombinant vector comprising a polynucleotide of claim 1 or claim 2 (claim 5);

a transformed host cell produced by transforming a host cell with a recombinant vector comprising a polynucleotide of claim 1 or claim 2 (claim 7);

The specification teaches as set forth above.



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The teaching of the specification cannot be extrapolated to enable the scope of the claims because one of skill in the art would not know how to use a polynucleotide that encodes a polypeptide of SEQ ID NO:1 because there is no showing a that polynucleotide other than SEQ ID NO:2 is overexpressed. Further, for the reasons set forth in Paragraph 6 above, one of skill in the art would not know how to use the encoded polypeptide if the polypeptide were not overexpressed in primary cancers because no function for SEQ ID NO:1 is taught in the specification. Thus, one of skill in the art would not know how to use a polynucleotide that encodes the polypeptide of SEQ ID NO:1, other than the polynucleotide of SEQ ID NO:2.

7. Claim 10 is rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

The claims are drawn to a process for producing a recombinant oncogenic protein comprising an amino acid sequence of SEQ ID NO:1 comprising the steps of (i) transforming a host cell with a recombinant vector comprising a polynucleotide encoding an oncogenic protein with the amino acid sequence of SEQ ID NO:1, thereby creating a transformed cell, (ii) culturing the transformed cell whereby the transformed cell produces said recombinant oncogenic protein, and (iii) collecting said recombinant polypeptide from the culture.

Although drawn to the DNA arts, the finding in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that “[a] written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” Id. At 1567, 43 USPQ2d at 1405. The court also stated that

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a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, and the holdings of those cases are also applicable to claims such as those at issue here. A

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disclosure that does not adequately describe a product itself logically cannot adequately describe a method of making that product.

Thus, the instant specification may provide an adequate written description of “an amino acid sequence of SEQ ID NO:1” per Lilly by structurally describing a representative number of species of “an amino acid sequence of SEQ ID NO:1” or by describing “structural features common to the members of the genus, which features constitute a substantial portion of the genus.” Alternatively, per Enzo, the specification can show that the claimed invention is complete “by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.”

In this case, the specification does not describe of “an amino acid sequence of SEQ ID NO:1”, in the method of claim 10, in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any “an amino acid sequence of SEQ ID NO:1”, nor does the specification provide any partial structure of such of “an amino acid sequence of SEQ ID NO:1”, nor any physical or chemical characteristics of the of “an amino acid sequence of SEQ ID NO:1”, nor any functional characteristics coupled with a known or disclosed correlation between structure and function, other than SEQ ID NO:1. Although the specification discloses a single polypeptide in SEQ ID NO:1, this does not provide a description of “an amino acid sequence of SEQ ID NO:1” of the claimed methods that would satisfy the standard set out in Enzo.

The specification also fails to describe the claimed of “an amino acid sequence of SEQ ID NO:1” by the test set out in Lilly. The specification describes only a single polypeptide, the polypeptide of SEQ ID NO:1. Therefore, it necessarily fails to describe a “representative number” of such species. In addition, the specification also does not describe “structural features common to the members of the genus, which features constitute a substantial portion of the genus.”

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Thus, the specification does not provide an adequate written description of "an amino acid sequence of SEQ ID NO:1". Since the specification fails to adequately describe the claimed product to be produced, it also fails to adequately describe the method of making that product.

***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 1, 2, 5, 7, and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagase et al. (1996, DNA Research 3:321-329), as evidenced by Genbank Accession No. D87450 .

The claims are drawn to the following:

an isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide represented by SEQ ID NO:1 (claim 1);

an isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide represented by SEQ ID NO:1 (claim 2), comprising the nucleotide sequence set forth in SEQ ID NO:2;

a recombinant vector comprising a polynucleotide of claim 1 or claim 2 (claim 5);

a transformed host cell produced by transforming a host cell with a recombinant vector comprising a polynucleotide of claim 1 or claim 2 (claim 7);

a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence of SEQ ID NO:2, wherein said polynucleotide has at least a length of 15 to 300 bases (claim 15);

a hybridization kit comprising the polynucleotide of claim 15 (claim 16);

a kit for detecting expression of mRNA which is translated into an oncogenic protein comprising the amino acid sequence of SEQ ID NO:1, comprising the polynucleotide of claim 15 (claim 17);

Nagase et al. disclosed the isolation and sequencing of a cDNA clone (KIAA0261) from the human immature myeloid cell line (abstract, page 325). As evidenced by the Genbank Accession No. D87450, and as shown by the attached sequence comparison between the nucleotide sequence of D87450 and the polypeptide sequence of SEQ ID NO:1 (Appendix A) and the attached sequence comparison between the nucleotide sequence of D87450 and the nucleotide sequence of SEQ ID NO:2, the isolated cDNA clone KIAA0261 comprises a sequence that is 100% identical to SEQ ID NO:2 and encodes a polypeptide having a sequence that is 100% identical to SEQ ID NO:1. It is noted that a cDNA clone comprising the sequence detailed in Genbank Accession No. D87450 would necessarily comprise "a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence of SEQ ID NO:2, wherein said polynucleotide has at least a length of 15 to 300 bases", as specified in claims 15-17. Thus, all of the claim limitations of claims 1, 2, 5, 7, and 15-17 are met.

### **Claim Rejections - 35 USC § 103**

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious

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at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagase et al. (1996, DNA Research 3:321-329), as evidenced by Genbank Accession No. D87450.

The claims are drawn to the following:

a hybridization kit comprising a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence of SEQ ID NO:2, wherein said polynucleotide has at least a length of 15 to 300 bases the polynucleotide of claim 15 (claim 16);

a kit for detecting expression of mRNA which is translated into an oncogenic protein comprising the amino acid sequence of SEQ ID NO:1, comprising a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence of SEQ ID NO:2, wherein said polynucleotide has at least a length of 15 to 300 bases (claim 17).

Nagase et al. teaches as set forth above but does not specifically teach a kit comprising a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence of SEQ ID NO:2, wherein said polynucleotide has at least a length of 15 to 300 bases.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make a kit useful for the detection of KIAA0261 expression because Nagase teaches that the KIAA0261 was an expressed human RNA that encodes a protein. Official notice is taken that hybridization probes typically comprise at least 15 bases and that one of skill in the art would have had a reasonable expectation of success in making the kit because hybridization probes were well known in the art to be used successfully.

12. Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagase et al. (1996, DNA Research 3:321-329), as evidenced by Genbank Accession No. D87450, in view of (Savvas, 1999, Protein Expression and Purification 17:183-202).

The claims are the following:

a process for producing a recombinant polypeptide or its salts comprising the amino acid sequence of SEQ ID NO:1 comprising the steps of:

transforming a host cell with a recombinant vector comprising a polynucleotide encoding the polypeptide represented by SEQ ID NO:1, thereby creating a transformed cell;

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culturing the transformed cell whereby the transformed cell produces said polypeptide; and

collecting said recombinant polypeptide from the culture (claim 9);

and

a process for producing a recombinant oncogenic protein comprising an amino acid sequence of SEQ ID NO:1 comprising the steps of:

transforming a host cell with a recombinant vector comprising a polynucleotide encoding an oncogenic protein with the amino acid sequence of SEQ ID NO:1, thereby creating a transformed cell;

culturing the transformed cell whereby the transformed cell produces said recombinant oncogenic protein; and

collecting said recombinant polypeptide from the culture (claim 10);

Nagase teaches as set forth above, but does not specifically teach a process for producing protein comprising culturing transformed cells.

Savvas teaches that vectors for gene expression can be used to produce proteins from cultured mammalian cells (page 183) and that fusion proteins may be employed to facilitate the secretion of the protein and the isolation of the protein.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the protein encoded by the KIAA0261 using the methods described by Savvas. One of skill in the art would have been motivated to produce the protein to make antibodies to study the expression of the protein because Nagase teaches that the KIAA0261 protein was expressed in a variety of human tissues. One of skill in the art would have had a reasonable expectation of success in producing the protein because of the success taught by Savvas in producing protein from cloned genes.



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13. Claim 18 is allowed. The closest prior art is Genbank Accession No. D87450 which discloses the sequence of SEQ ID NO:2. However, the reference does not disclose the specific primer set of the polynucleotides having the sequences of SEQ ID NO:8 and SEQ ID NO:9.

### Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine M. Joyce whose telephone number is 571-272-3321. The examiner can normally be reached on Monday thru Friday, 10:15 - 6:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
JEFFREY SIEW  
SUPERVISORY PATENT EXAMINER

Catherine Joyce  
Examiner  
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Appendix A, pg. 2

## RESULT 2

D87450

LOCUS D87450 6155 bp mRNA linear PRI 06-OCT-2001

DEFINITION Human mRNA for KIAA0261 gene, partial cds.

ACCESSION D87450

VERSION D87450.1 GI:1665788

KEYWORDS KIAA0261.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;  
Hominidae; Homo.

## REFERENCE 1

AUTHORS Nagase,T., Seki,N., Ishikawa,K., Ohira,M., Kawarabayasi,Y.,  
Ohara,O., Tanaka,A., Kotani,H., Miyajima,N. and Nomura,N.TITLE Prediction of the coding sequences of unidentified human genes. VI.  
The coding sequences of 80 new genes (KIAA0201-KIAA0280) deduced by  
analysis of cDNA clones from cell line KG-1 and brain

JOURNAL DNA Res. 3 (5), 321-329 (1996)

PUBMED 9039502

## REFERENCE 2 (bases 1 to 6155)

AUTHORS Ohara,O., Nagase,T., Kikuno,R. and Nomura,N.

TITLE Direct Submission

JOURNAL Submitted (27-AUG-1996) Osamu Ohara, Kazusa DNA Research Institute;  
1532-3, Yana, Kisarazu, Chiba 292-0812, Japan  
(E-mail:cdnainfo@kazusa.or.jp, Tel:+81-438-52-3913)

## FEATURES Location/Qualifiers

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Appendix A, pg. 2

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## ORIGIN

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Best Local Similarity:	100.0%	Mismatches:	0
Query Match:	100.0%	Indels:	0
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US-10-758-562-1 (1-1190) x D87450 (1-6155)

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Db	474	AAACCTAAAGTGAAGAAGAAAGTACTGGAGATCCTTTTGGATTTGATAGTGATGATGAG	533
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Qy	101	SerGluAlaAlaGlnLeuGluGluValThrSerValLeuGluAlaAsnSerLysIleSer	120
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Qy	121	HisValValValGluAspThrValValSerAspLysCysPheProLeuGluAspThrLeu	140
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Qy	161	AsnLysLeuIleThrSerAspLysValGluAsnPheHisGluGluHisGluLysAsnSer	180
Db	774	AATAAATTAATAACTTCAGATAAAGTGGAGAATTTTCATGAAGAACATGAAAAGAATAGT	833
Qy	181	HisHisIleHisLysAsnAlaAspAspSerThrLysLysProAsnAlaGluThrThrVal	200
Db	834	CACCATATTCACAAAAATGCTGATGACAGTACTAAGAAACCAATGCAGAACTACAGTG	893
Qy	201	AlaSerGluIleLysGluThrAsnAspThrTrpAsnSerGlnPheGlyLysArgProGlu	220

Appendix A, pg. 3

Db	894		GCTTCTGAAATCAAGGAAACAAATGATACCTGGAACCTCCAGTTTGGGAAAAGGCCAGAA	953
Qy	221		SerProSerGluIleSerProIleLysGlySerValArgThrGlyLeuPheGluTrpAsp	240
Db	954		TCACCATCAGAAATATCTCCAATCAAGGGATCTGTAGAACTGGTTTGGTTTGAATGGGAT	1013
Qy	241		AsnAspPheGluAspIleArgSerGluAspCysIleLeuSerLeuAspSerAspProLeu	260
Db	1014		AATGATTTTGAAGATATCAGATCAGAAGACTGTATTTTAAGTTTGGATAGTGATCCCCTT	1073
Qy	261		LeuGluMetLysAspAspAspPheLysAsnArgLeuGluAsnLeuAsnGluAlaIleGlu	280
Db	1074		TTGGAGATGAAGGATGACGATTTTAAAAATCGATTGGAAAATCTGAATGAAGCCATTGAG	1133
Qy	281		GluAspIleValGlnSerValLeuArgProThrAsnCysArgThrTyrCysArgAlaAsn	300
Db	1134		GAAGATATTGTACAAAGTGTTCTTAGGCCAACCACTGTAGGACGTACTGTAGGGCCAAT	1193
Qy	301		LysThrLysSerSerGlnGlyAlaSerAsnPheAspLysLeuMetAspGlyThrSerGln	320
Db	1194		AAAACGAAATCCTCCCAAGGAGCATCAAATTTTGATAAGCTGATGGACGGCACCAGTCAG	1253
Qy	321		AlaLeuAlaLysAlaAsnSerGluSerSerLysAspGlyLeuAsnGlnAlaLysLysGly	340
Db	1254		GCCTTAGCCAAAGCAAACAGTGAATCGAGTAAAGATGGCCTGAATCAGGCAAAGAAAGGG	1313
Qy	341		GlyValSerCysGlyThrSerPheArgGlyThrValGlyArgThrArgAspTyrThrVal	360
Db	1314		GGTGTAAGTTGTGGGACCAGTTTTAGAGGGACAGTTGGACGGACTAGAGATTACACTGTT	1373
Qy	361		LeuHisProSerCysLeuSerValCysAsnValThrIleGlnAspThrMetGluArgSer	380
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Qy	381		MetAspGluPheThrAlaSerThrProAlaAspLeuGlyGluAlaGlyArgLeuArgLys	400
Db	1434		ATGGATGAGTTCACTGCATCCACTCCTGCAGATTTGGGAGAAGCTGGTCTCTCAGAAAA	1493
Qy	401		LysAlaAspIleAlaThrSerLysThrThrThrArgPheArgProSerAsnThrLysSer	420
Db	1494		AAGGCAGATATTGCAACTTCTAAGACTACTACTAGATTTTCGACCTAGTAATACTAAATCC	1553
Qy	421		LysLysAspValLysLeuGluPhePheGlyPheGluAspHisGluThrGlyGlyAspGlu	440
Db	1554		AAAAAGGATGTTAAACTTGAATTTTTTGTTTTGAAGATCATGAGACAGGAGGTGATGAA	1613
Qy	441		GlyGlySerGlySerSerAsnTyrLysIleLysTyrPheGlyPheAspAspLeuSerGlu	460
Db	1614		GGAGGTTCTGGAAGTTCTAATTACAAAATTAAGTATTTTGGCTTTGATGATCTCAGTGAA	1673
Qy	461		SerGluAspAspGluAspAspAspCysGlnValGluArgLysThrSerLysLysArgThr	480
Db	1674		AGCGAAGATGATGAAGATGATGACTGTCAAGTAGAAAGAAAGACAAGCAAAAAAAGAACT	1733
Qy	481		LysThrAlaProSerProSerLeuGlnProProProGluSerAsnAspAsnSerGlnAsp	500
Db	1734		AAAACAGCTCCATCACCTCCTTGCGAGCCTCCCCAGAAAGCAATGATAATTCCCAGGAC	1793
Qy	501		SerGlnSerGlyThrAsnAsnAlaGluAsnLeuAspPheThrGluAspLeuProGlyVal	520

Appendix A, Pg. 4

Db	1794	AGTCAGTCTGGTACTAACAATGCAGAAAACCTTGGATTTTACAGAGGACTTGCCTGGTGTG	1853
Qy	521	ProGluSerValLysLysProIleAsnLysGlnGlyAspLysSerLysGluAsnThrArg	540
Db	1854	CCTGAAAGTGTGAAGAAGCCCATAAATAAACAGGAGATAAATCAAAGGAAAATACCAGA	1913
Qy	541	LysIlePheSerGlyProLysArgSerProThrLysAlaValTyrAsnAlaArgHisTrp	560
Db	1914	AAGATTTTGTAGTGGCCCCAAACGGTCACCCACAAAAGCTGTATATAATGCCAGACATTGG	1973
Qy	561	AsnHisProAspSerGluGluLeuProGlyProProValValLysProGlnSerValThr	580
Db	1974	AATCATCCAGATTGAGAAGAACTGCCTGGGCCACCAGTAGTAAACCTCAGAGTGTACACA	2033
Qy	581	ValArgLeuSerSerLysGluProAsnGlnLysAspAspGlyValPheLysAlaProAla	600
Db	2034	GTGAGGCTGTCTTCAAAGGAACCAATCAAAAAGATGATGGAGTTTTTAAGGCTCCTGCA	2093
Qy	601	ProProSerLysValIleLysThrValThrIleProThrGlnProTyrGlnAspIleVal	620
Db	2094	CCACCATCCAAAGTGATAAAACTGTGACAATACCTACTCAGCCCTACCAAGATATAGTT	2153
Qy	621	ThrAlaLeuLysCysArgArgGluAspLysGluLeuTyrThrValValGlnHisValLys	640
Db	2154	ACTGCACTGAAATGCAGACGAGAAGACAAAGAATTATATACTGTTGTTTCAGCACGTGAAG	2213
Qy	641	HisPheAsnAspValValGluPheGlyGluAsnGlnGluPheThrAspAspIleGluTyr	660
Db	2214	CACTTCAACGATGTTGTAGAATTTGGTGAAAATCAAGAGTTCAGTATGACATTGAGTAC	2273
Qy	661	LeuLeuSerGlyLeuLysSerThrGlnProLeuAsnThrArgCysLeuSerValIleSer	680
Db	2274	TTGTTAAGTGGCTTAAAGAGCACTCAGCCTCTAAACACACGTTGCCTTAGTGTTATTAGC	2333
Qy	681	LeuAlaThrLysCysAlaMetProSerPheArgMetHisLeuArgAlaHisGlyMetVal	700
Db	2334	TTGGCTACTAAATGTGCCATGCCAGTTTTCGAATGCACCTGAGAGCACATGGGATGGTA	2393
Qy	701	AlaMetValPheLysThrLeuAspAspSerGlnHisHisGlnAsnLeuSerLeuCysThr	720
Db	2394	GCAATGGTCTTTAAACCTTGGATGATTCCAGCACCATCAGAATCTGTCCCTCTGTACA	2453
Qy	721	AlaAlaLeuMetTyrIleLeuSerArgAspArgLeuAsnMetAspLeuAspArgAlaSer	740
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Qy	741	LeuAspLeuMetIleArgLeuLeuGluLeuGluGlnAspAlaSerSerAlaLysLeuLeu	760
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Qy	761	AsnGluLysAspMetAsnLysIleLysGluLysIleArgArgLeuCysGluThrValHis	780
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Db	2634	AACAAGCATCTTGATCTAGAAAATATAACGACTGGGCATTTAGCTATGGAGACATTATTA	2693
Qy	801	SerLeuThrSerLysArgAlaGlyAspTrpPheLysGluGluLeuArgLeuLeuGlyGly	820
Db	2694	TCCCTTACTTCTAAACGAGCAGGAGACTGGTTTAAAGAAGAACTCCGGCTTTTGGGTGGT	2753

Appendix A, pg. 5

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Db	2814	GAAGAGAAACTGGTAGCCTCACTATGGGGAGCAGAGAGATGTTTACGAGTTTTAGAAAGT	2873
Qy	861	ValThrValHisAsnProGluAsnGlnSerTyrLeuIleAlaTyrLysAspSerGlnLeu	880
Db	2874	GTAAGTGTGCATAATCCCGAAAATCAAAGCTACTTGATAGCATATAAAGATTCCCAACTT	2933
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Qy	901	AlaGluAspSerIleCysLeuAlaAspSerLysProLeuProHisGlnAsnValThrAsn	920
Db	2994	GCTGAGGACAGCATATGCTTAGCTGACAGTAAGCCTCTGCCTCACCAGAATGTAACAACT	3053
Qy	921	HisValGlyLysAlaValGluAspCysMetArgAlaIleIleGlyValLeuLeuAsnLeu	940
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Qy	941	ThrAsnAspAsnGluTrpGlySerThrLysThrGlyGluGlnAspGlyLeuIleGlyThr	960
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Qy	961	AlaLeuAsnCysValLeuGlnValProLysTyrLeuProGlnGluGlnArgPheAspIle	980
Db	3174	GCGCTGAAGTGTGTGCTTCAGGTTCCAAAGTACCTACCTCAGGAGCAGAGATTTGATATT	3233
Qy	981	ArgValLeuGlyLeuGlyLeuLeuIleAsnLeuValGluTyrSerAlaArgAsnArgHis	1000
Db	3234	CGAGTGCTGGGCTTAGGTCTGCTGATAAATCTAGTGAGATATAGTGCTCGGAATCGGCAC	3293
Qy	1001	CysLeuValAsnMetGluThrSerCysSerPheAspSerSerIleCysSerGlyGluGly	1020
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Db	3474	GCTCCCACTCAGCATGATAAGAGTGGAGAGTGGCAAGAAACAAGTGGAGAAATACAG	3533
Qy	1081	TrpValSerThrGluLysThrAspGlyThrGluGluLysHisLysLysGluGluGluAsp	1100
Db	3534	TGGGTGTCAACTGAAAAGACTGATGGTACAGAAGAGAAACATAAGAAGGAGGAGGAGAT	3593
Qy	1101	GluGluLeuAspLeuAsnLysAlaLeuGlnHisAlaGlyLysHisMetGluAspCysIle	1120
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Appendix A, pg. 4

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Qy	1161	LysPheLeuSerPheMetAsnLeuThrCysAlaValGlyThrThrGlyGlnLysSerIle	1180
Db	3774	AAATTTTGTGAGTTTATGAATCTCACTTGTGCTGTTGGAACAACACTGGCCAGAAATCTATC	3833
Qy	1181	SerArgValIleGluTyrLeuGluHisCys	1190
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Appendix B, ps 1

RESULT 2  
D87450

LOCUS D87450 6155 bp mRNA linear PRI 06-OCT-2001

DEFINITION Human mRNA for KIAA0261 gene, partial cds.

ACCESSION D87450

VERSION D87450.1 GI:1665788

KEYWORDS KIAA0261.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens  
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;  
Hominidae; Homo.

REFERENCE 1

AUTHORS Nagase,T., Seki,N., Ishikawa,K., Ohira,M., Kawarabayasi,Y.,  
Ohara,O., Tanaka,A., Kotani,H., Miyajima,N. and Nomura,N.

TITLE Prediction of the coding sequences of unidentified human genes. VI.  
The coding sequences of 80 new genes (KIAA0201-KIAA0280) deduced by  
analysis of cDNA clones from cell line KG-1 and brain

JOURNAL DNA Res. 3 (5), 321-329 (1996)

PUBMED 9039502

REFERENCE 2 (bases 1 to 6155)

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TITLE Direct Submission

JOURNAL Submitted (27-AUG-1996) Osamu Ohara, Kazusa DNA Research Institute;  
1532-3, Yana, Kisarazu, Chiba 292-0812, Japan  
(E-mail:cdnainfo@kazusa.or.jp, Tel:+81-438-52-3913)

FEATURES

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Appendix B, ps. 2

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## ORIGIN

Query Match 100.0%; Score 3570; DB 5; Length 6155;  
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 Matches 3570; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy	61	GATGAAGTCTTTTCCAACAAACGGACTACCTTAGCACAAAATGGGGAGAGACCACATTT	120
Db	354	GATGAAGTCTTTTCCAACAAACGGACTACCTTAGCACAAAATGGGGAGAGACCACATTT	413
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Qy	241	TCTCTACCAGTTTCTTCAAAGAATTTAGCCCAGGTTAAGTGTTCCTCTTATTCAGAATCT	300
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Qy	301	AGTGAAGCTGCTCAGTTGGAAGAGGTCACITTCAGTACTTGAAGCTAATAGCAAAATTAGT	360
Db	594	AGTGAAGCTGCTCAGTTGGAAGAGGTCACITTCAGTACTTGAAGCTAATAGCAAAATTAGT	653
Qy	361	CATGTGGTTCGTTGAAGACACTGTCGTTTCTTGATAAAATGCTTCCCTTTGGAGGACACTTTA	420
Db	654	CATGTGGTTCGTTGAAGACACTGTCGTTTCTTGATAAAATGCTTCCCTTTGGAGGACACTTTA	713
Qy	421	CTTGGGAAAGAAAAGAGCACAAACCGAATTGTAGAAGATGATGCAAGCATAAGTAGCTGT	480
Db	714	CTTGGGAAAGAAAAGAGCACAAACCGAATTGTAGAAGATGATGCAAGCATAAGTAGCTGT	773
Qy	481	AATAAAATTAATAACTTCAGATAAAGTGGAGAATTTTCATGAAGAACATGAAAAGAATAGT	540
Db	774	AATAAAATTAATAACTTCAGATAAAGTGGAGAATTTTCATGAAGAACATGAAAAGAATAGT	833
Qy	541	CACCATATTCACAAAAATGCTGATGACAGTACTAAGAAACCAATGCAGAACTACAGTG	600
Db	834	CACCATATTCACAAAAATGCTGATGACAGTACTAAGAAACCAATGCAGAACTACAGTG	893
Qy	601	GCTTC'TGAAATCAAGGAAACAAATGATACTTGGAACTCCCAGTTTGGGAAAAGGCCAGAA	660
Db	894	GCTTC'TGAAATCAAGGAAACAAATGATACTTGGAACTCCCAGTTTGGGAAAAGGCCAGAA	953
Qy	661	TCACCATCAGAAATATCTCCAATCAAGGGATCTGTAGAACTGGTTTGTGTTGAATGGGAT	720
Db	954	TCACCATCAGAAATATCTCCAATCAAGGGATCTGTAGAACTGGTTTGTGTTGAATGGGAT	1013

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Qy	721	AATGATTTTGAAGATATCAGATCAGAAGACTGTATTTTAAAGTTTGGATAGTGATCCCCCTT	780
Db	1014	AATGATTTTGAAGATATCAGATCAGAAGACTGTATTTTAAAGTTTGGATAGTGATCCCCCTT	1073
Qy	781	TTGGAGATGAAGGATGACGATTTTAAAAATCGATTGGAAAATCTGAATGAAGCCATTGAG	840
Db	1074	TTGGAGATGAAGGATGACGATTTTAAAAATCGATTGGAAAATCTGAATGAAGCCATTGAG	1133
Qy	841	GAAGATATTGTACAAAGTGTTCCTTAGGCCAACCAACTGTAGGACGTACTGTAGGGCCAAT	900
Db	1134	GAAGATATTGTACAAAGTGTTCCTTAGGCCAACCAACTGTAGGACGTACTGTAGGGCCAAT	1193
Qy	901	AAAACGAAATCCTCCCAAGGAGCATCAAATTTTGATAAGCTGATGGACGGCACCAGTCAG	960
Db	1194	AAAACGAAATCCTCCCAAGGAGCATCAAATTTTGATAAGCTGATGGACGGCACCAGTCAG	1253
Qy	961	GCCCTTAGCCAAAGCAAACAGTGAATCGAGTAAAGATGGCCTGAATCAGGCAAAGAAAGGG	1020
Db	1254	GCCCTTAGCCAAAGCAAACAGTGAATCGAGTAAAGATGGCCTGAATCAGGCAAAGAAAGGG	1313
Qy	1021	GGTGTAAAGTTGTGGGACCAGTTTTFAGAGGGACAGTTGGACGGACTAGAGATTACACTGTT	1080
Db	1314	GGTGTAAAGTTGTGGGACCAGTTTTFAGAGGGACAGTTGGACGGACTAGAGATTACACTGTT	1373
Qy	1081	TTACATCCATCTTGCTTGTTCAGTTTGTAAATGTTACCATACAGGATACTATGGAACGCAGC	1140
Db	1374	TTACATCCATCTTGCTTGTTCAGTTTGTAAATGTTACCATACAGGATACTATGGAACGCAGC	1433
Qy	1141	ATGGATGAGTTCACTGCATCCACTCCTGCAGATTTGGGAGAAGCTGGTCGTCTCAGAAAA	1200
Db	1434	ATGGATGAGTTCACTGCATCCACTCCTGCAGATTTGGGAGAAGCTGGTCGTCTCAGAAAA	1493
Qy	1201	AAGGCAGATATTTGCAACTTCTAAGACTACTACTAGATTTTCGACCTAGTAATACTAAATCC	1260
Db	1494	AAGGCAGATATTTGCAACTTCTAAGACTACTACTAGATTTTCGACCTAGTAATACTAAATCC	1553
Qy	1261	AAAAAGGATGTTAAACTTGAATTTTTTGGTTTTGAAGATCATGAGACAGGAGGTGATGAA	1320
Db	1554	AAAAAGGATGTTAAACTTGAATTTTTTGGTTTTGAAGATCATGAGACAGGAGGTGATGAA	1613
Qy	1321	GGAGGTTCTGGAAGTTCTAATTACAAAATTAAGTATTTTGGCTTTGATGATCTCAGTGAA	1380
Db	1614	GGAGGTTCTGGAAGTTCTAATTACAAAATTAAGTATTTTGGCTTTGATGATCTCAGTGAA	1673
Qy	1381	AGCGAAGATGATGAAGATGATGACTGTCAAGTAGAAAAGAAAGACAAGCAAAAAAAGAAGT	1440
Db	1674	AGCGAAGATGATGAAGATGATGACTGTCAAGTAGAAAAGAAAGACAAGCAAAAAAAGAAGT	1733
Qy	1441	AAAACAGCTCCATCACCTCCTTGCAGCCTCCCCAGAAAGCAATGATAATTCCCAGGAC	1500
Db	1734	AAAACAGCTCCATCACCTCCTTGCAGCCTCCCCAGAAAGCAATGATAATTCCCAGGAC	1793
Qy	1501	AGTCAGTCTGGTACTAACAATGCAGAAAACCTTGGATTTTACAGAGGACTTGCCTGGTGTG	1560
Db	1794	AGTCAGTCTGGTACTAACAATGCAGAAAACCTTGGATTTTACAGAGGACTTGCCTGGTGTG	1853
Qy	1561	CTTGAAAGTGTGAAGAAGCCCATAAATAAACAAGGAGATAAATCAAAGGAAAATACCAGA	1620
Db	1854	CTTGAAAGTGTGAAGAAGCCCATAAATAAACAAGGAGATAAATCAAAGGAAAATACCAGA	1913

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Qy	1621	AAGATTTT TAGTGGCCCCAAACGGTCACCCACAAAAGCTGTATATAATGCCAGACATTGG	1680
Db	1914	AAGATTTT TAGTGGCCCCAAACGGTCACCCACAAAAGCTGTATATAATGCCAGACATTGG	1973
Qy	1681	AATCATCCAGATT CAGAAGAACTGCCTGGGCCACCAGTAGTAAAACCTCAGAGTGT CACA	1740
Db	1974	AATCATCCAGATT CAGAAGAACTGCCTGGGCCACCAGTAGTAAAACCTCAGAGTGT CACA	2033
Qy	1741	GTGAGGCTGTCTTCAAAGGAACCAAATCAAAAAGATGATGGAGTTTTTAAGGCTCCTGCA	1800
Db	2034	GTGAGGCTGTCTTCAAAGGAACCAAATCAAAAAGATGATGGAGTTTTTAAGGCTCCTGCA	2093
Qy	1801	CCACCATCCAAAGTGATAAAAACTGTGACAATACCTACTCAGCCCTACCAAGATATAGTT	1860
Db	2094	CCACCATCCAAAGTGATAAAAACTGTGACAATACCTACTCAGCCCTACCAAGATATAGTT	2153
Qy	1861	ACTGCACTGAAATGCAGACGAGAAGACAAAGAAATTATATACTGTTGTT CAGCACGTGAAG	1920
Db	2154	ACTGCACTGAAATGCAGACGAGAAGACAAAGAAATTATATACTGTTGTT CAGCACGTGAAG	2213
Qy	1921	CACCTTCAACGATGTTGTAGAAATTTGGTGAAAATCAAGAGTTCACTGATGACATTGAGTAC	1980
Db	2214	CACCTTCAACGATGTTGTAGAAATTTGGTGAAAATCAAGAGTTCACTGATGACATTGAGTAC	2273
Qy	1981	TTGTTAAGTGGCTTAAAGAGCACTCAGCCTCTAAACACACGTTGCCTTAGTGTTATTAGC	2040
Db	2274	TTGTTAAGTGGCTTAAAGAGCACTCAGCCTCTAAACACACGTTGCCTTAGTGTTATTAGC	2333
Qy	2041	TTGGCTACTAAATGTGCCATGCCAGTTTTCGAATGCACCTGAGAGCACATGGGATGGTA	2100
Db	2334	TTGGCTACTAAATGTGCCATGCCAGTTTTCGAATGCACCTGAGAGCACATGGGATGGTA	2393
Qy	2101	GCAATGGTCTTTAAACCTTGGATGATTTCCAGCACCATCAGAATCTGTCCCTCTGTACA	2160
Db	2394	GCAATGGTCTTTAAACCTTGGATGATTTCCAGCACCATCAGAATCTGTCCCTCTGTACA	2453
Qy	2161	GCTGCCCTCATGTATATACTGAGTAGAGATCGTTTGAACATGGATCTTGATAGAGCTAGC	2220
Db	2454	GCTGCCCTCATGTATATACTGAGTAGAGATCGTTTGAACATGGATCTTGATAGAGCTAGC	2513
Qy	2221	TTAGATCTAATGATTCGACTTTTGGAACTGGAACAAGATGCTTCATCAGCCAAGCTACTG	2280
Db	2514	TTAGATCTAATGATTCGACTTTTGGAACTGGAACAAGATGCTTCATCAGCCAAGCTACTG	2573
Qy	2281	AATGAAAAAGACATGAACAAAATTAAAGAAAAAATCCGAAGGCTCTGTGAAACTGTACAC	2340
Db	2574	AATGAAAAAGACATGAACAAAATTAAAGAAAAAATCCGAAGGCTCTGTGAAACTGTACAC	2633
Qy	2341	AACAAGCATCTTGATCTAGAAAATATAACGACTGGGCATTTAGCTATGGAGACATTATTA	2400
Db	2634	AACAAGCATCTTGATCTAGAAAATATAACGACTGGGCATTTAGCTATGGAGACATTATTA	2693
Qy	2401	TCCCTTACTTCTAAACGAGCAGGAGACTGGTTTAAAGAAGAACTCCGGCTTTTGGGTGGT	2460
Db	2694	TCCCTTACTTCTAAACGAGCAGGAGACTGGTTTAAAGAAGAACTCCGGCTTTTGGGTGGT	2753
Qy	2461	CTGGATCATATTTGTAGATAAAGTAAAAGAATGTGTGGATCATTTAAGTAGAGATGAGGAT	2520
Db	2754	CTGGATCATATTTGTAGATAAAGTAAAAGAATGTGTGGATCATTTAAGTAGAGATGAGGAT	2813
Qy	2521	GAAGAGAAACTGGTAGCCTCACTATGGGGAGCAGAGAGATGTTTACGAGTTT TAGAAAGT	2580

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Db	2814	GAAGAGAACTGGTAGCCTCACTATGGGGAGCAGAGAGATGTTTACGAGTTTTAGAAAGT	2873
Qy	2581	GTAAGTGTGCATAAATCCCGAAAATCAAAGCTACTTGATAGCATATAAAGATTCCCAACTT	2640
Db	2874	GTAAGTGTGCATAAATCCCGAAAATCAAAGCTACTTGATAGCATATAAAGATTCCCAACTT	2933
Qy	2641	ATTGTTTTCATCAGCTAAAGCATTACAGCATTTGTAAGAAGTGAATTCAGCAGTACAACCGT	2700
Db	2934	ATTGTTTTCATCAGCTAAAGCATTACAGCATTTGTAAGAAGTGAATTCAGCAGTACAACCGT	2993
Qy	2701	GCTGAGGACAGCATATGCTTAGCTGACAGTAAGCCCTGCGCTCACCAGAATGTAACATAAC	2760
Db	2994	GCTGAGGACAGCATATGCTTAGCTGACAGTAAGCCCTGCGCTCACCAGAATGTAACATAAC	3053
Qy	2761	CATGTAGGCAAAGCAGTGGAGGACTGCATGAGGGCCATCATCGGGGTGTTGCTTAATTTA	2820
Db	3054	CATGTAGGCAAAGCAGTGGAGGACTGCATGAGGGCCATCATCGGGGTGTTGCTTAATTTA	3113
Qy	2821	ACTAATGATAATGAGTGGGGCAGCACCAAAACAGGAGAGCAGGACGGTCTCATAGGCACA	2880
Db	3114	ACTAATGATAATGAGTGGGGCAGCACCAAAACAGGAGAGCAGGACGGTCTCATAGGCACA	3173
Qy	2881	GCGCTGAAGTGTGTGCTTCAGGTTCCAAAGTACCTACCTCAGGAGCAGAGATTTGATATT	2940
Db	3174	GCGCTGAAGTGTGTGCTTCAGGTTCCAAAGTACCTACCTCAGGAGCAGAGATTTGATATT	3233
Qy	2941	CGAGTGCTGGGCTTAGGTCTGCTGATAAATCTAGTGGAGTATAGTGCTCGGAATCGGCAC	3000
Db	3234	CGAGTGCTGGGCTTAGGTCTGCTGATAAATCTAGTGGAGTATAGTGCTCGGAATCGGCAC	3293
Qy	3001	TGTCCTGTCAACATGGAAACATCGTGCTCTTTTGATTTCTTCCATCTGTAGTGGAGAAGGG	3060
Db	3294	TGTCCTGTCAACATGGAAACATCGTGCTCTTTTGATTTCTTCCATCTGTAGTGGAGAAGGG	3353
Qy	3061	GATGATAGTTTAAGGATAGGTGGACAAGTTCATGCTGTCCAGGCTTTAGTGCAGCTATTTC	3120
Db	3354	GATGATAGTTTAAGGATAGGTGGACAAGTTCATGCTGTCCAGGCTTTAGTGCAGCTATTTC	3413
Qy	3121	CTTGAGCGAGAGCGGGCAGCCAGCTAGCAGAAAGTAAAACAGATGAGTTGATCAAAGAT	3180
Db	3414	CTTGAGCGAGAGCGGGCAGCCAGCTAGCAGAAAGTAAAACAGATGAGTTGATCAAAGAT	3473
Qy	3181	GCTCCCACCACTCAGCATGATAAGAGTGGAGAGTGGCAAGAAACAAGTGGAGAAATACAG	3240
Db	3474	GCTCCCACCACTCAGCATGATAAGAGTGGAGAGTGGCAAGAAACAAGTGGAGAAATACAG	3533
Qy	3241	TGGGTGTCAACTGAAAAGACTGATGGTACAGAAGAGAAACATAAGAAGGAGGAGGAGGAT	3300
Db	3534	TGGGTGTCAACTGAAAAGACTGATGGTACAGAAGAGAAACATAAGAAGGAGGAGGAGGAT	3593
Qy	3301	GAAGAAGTTGACCTCAATAAAGCCCTTCAGCATGCCGGCAAACACATGGAGGATTGCATT	3360
Db	3594	GAAGAAGTTGACCTCAATAAAGCCCTTCAGCATGCCGGCAAACACATGGAGGATTGCATT	3653
Qy	3361	GTGGCCTCCTACACGGCACTACTTCTTGGGTGTCTCTGCCAGGAAAGTCCAATCAATGTA	3420
Db	3654	GTGGCCTCCTACACGGCACTACTTCTTGGGTGTCTCTGCCAGGAAAGTCCAATCAATGTA	3713
Qy	3421	ACCACGTGCGGGAATATCTGCCAGAAGGAGACTTTTCAATAATGACAGAGATGCTCAA	3480

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Db	3714	ACCACTGTGCGGGAATATCTGCCAGAAGGAGACTTTTCAATAATGACAGAGATGCTCAA	3773
Qy	3481	AAATTTTGTAGTTTTATGAATCTCACTTGTGCTGTTGGAACAACCTGGCCAGAAATCTATC	3540
Db	3774	AAATTTTGTAGTTTTATGAATCTCACTTGTGCTGTTGGAACAACCTGGCCAGAAATCTATC	3833
Qy	3541	TCTAGAGTGATTGAATATTTGGAACATTGC	3570
Db	3834	TCTAGAGTGATTGAATATTTGGAACATTGC	3863